BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

By the foregoing amendment, the specification has been amended to update the status of the now patented parent application. No new matter has been added.

Turning now to the Official Action, the Examiner has stated that "upon reconsideration" the restriction requirement has been withdrawn. However, the Examiner has maintained the election of species requirement.[1] Thus, the Examiner stated that claims 53-58, 62, 64-68, 92-94, and 96-101 have been withdrawn as being directed to a non-elected species. Claims 52, 59-61, 63, 69-91 and 95 have been noted as being examined on the merits.

Claims 52, 59-61, 63, 69-91 and 95 have been rejected under 35 U.S.C. § 112, first paragraph, for containing subject matter which allegedly was not described in the specification in such a way to enable one skilled in the art to make and/or use the claimed invention. This rejection is respectfully traversed.

The Examiner has asserted that applicants' disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without undue

---

[1] The Examiner has indicated that the applicants "did not distinctly and specifically point out the supposed errors in the restriction requirement . . . ." Office Action at 2, ¶1 (emphasis added). Applicants respectfully disagree. In the reply filed on October 27, 2003, Applicants set forth in detail the errors in the restriction requirement including the absence of a serious burden to examine all of the groups and providing specific reasoning as to why at least Group I and II should be examined together. Thus, the restriction requirement was properly traversed and should not be treated as being without traverse.

As to the election of species requirement (as opposed to the restriction requirement), applicants also specifically pointed out the unduly limiting nature of the election of species requirement. Thus, the election of species was also properly traversed and should not be treated as being without traverse.

experimentation. Office Action at 2. In particular, the Examiner indicated that the claims of the present application are intended for use in humans with respect to transplantation antigens as only humans undergo transplantation. Office Action at 3, 2nd paragraph. Applicants respectfully disagree since the claims of the present application are directed to antigens which include both transplantation antigens and autoantigens. Moreover, transplantation can be conducted in any mammal as desired, not simply limited to humans. Transplantation in veterinary medicine is becoming more commonplace. Thus, there is no reason to believe that the claimed invention should only be limited to humans.

Further, the Examiner has stated that as of 1994 there were no methods available for inducing oral tolerance to a transplantation antigen in a human. Office Action at 3, 1st paragraph. Applicants would agree with this statement in the context of the prior art as the present application for the first time discloses a method for suppressing or reducing the immune response of a mammal by administering the claimed plant tissue or plant tissue extract. However, the Examiner then contradicts himself by stating that some ten years later there were still no methods available for inducing oral tolerance to a transplantation antigen in a human but notes at least two exceptions. Nevertheless, applicants have adequately disclosed the claimed invention in the specification of the present application and, in addition, have conducted experiments demonstrating that transgenic plants expressing autoantigens fed to mice induced oral immune tolerance as described in the two declarations submitted by Dr. Jevnikar, an inventor of the claimed invention, in the parent application. A copy of both declarations are attached hereto.

The Examiner has also asserted that the present application does not provide any *in vivo* or *in vitro* data. It is well recognized by the Federal Circuit that *in vivo* testing is not necessary to satisfy § 112, first paragraph, as this confuses the requirements under the law for obtaining a patent with the requirements for obtaining government (FDA) approval to market a particular drug for human consumption. Moreover, as described above with regard to the declarations of Dr. Jevnikar, experiments have been conducted demonstrating that transgenic plants expressing autoantigens fed to mice induced oral immune response.

In view of the above, the present application provides sufficient enablement so that one skilled in the art could make and/or use the claimed invention without undue experimentation. Thus withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Additionally, claims 52, 59-61, 63, 69-91 and 95 have been rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Weiner et al. (WO 92/07581) in view of Lam et al. (U.S. Patent No. 5,484,719). This rejection is respectfully traversed.

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. *See, e.g., In re Fritch*, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). Here, absent the impermissible use of hindsight reconstruction, there is no teaching or suggestion to combine the references as proposed by the Examiner.

WO 92/07581 describes a method for suppressing an immune response in a recipient mammal by administering an agent such as splenocytes from the donor, splenic extracts thereof, and cultured lymphocytes from the donor, extracts of such cultured lymphocytes or MHC antigens or fragments thereof from the donor.

U.S. Patent No. 5,484,719 ("the '719 patent") discloses the use of transgenic plants to produce surface antigenic proteins characteristic of viruses, bacteria, fungi and parasite (column 5, lines 1-8). Example 1 of the '719 patent demonstrates the transgenic production for a small viral protein, hepatitis B surface antigen.

However, there is no suggestion in the '719 patent, or otherwise, that mammalian antigens could be produced in transgenic plants. Further, the '719 patent proposes the consumption of heterologous antigen-producing transgenic plants or plant materials as a vaccine, *i.e.*, oral consumption of these antigens to trigger an immune response. This teaches away from the presently claimed invention which involves the consumption of transgenic plants which produce mammalian antigens as a means of inducing tolerance for the relevant mammalian antigen. One of ordinary skill in the art would not be motivated by the '719 patent to take the approach of the present invention and nothing in the teachings of this cited patent suggests the claimed pharmaceutical compositions for suppressing or reducing the immune response of a mammal to a transplantation antigen or an autoantigen.

Furthermore, the Examiner has stated that the induction of tolerance and the induction of an immune response are "two sides of the same coin" and that some immunologists refer to the induction of tolerance as the induction of a suppressive immune response. Office Action at 5, 3rd paragraph. However, the Examiner has

not provided "any proof" that any immunologist would refer to induction of tolerance as the induction of a suppressive immune response. Without such "proof" the Examiner's statements are merely unsupported allegations. Also, it is evident from each of the teachings of the '719 patent and WO 92/07581 that this suggested teaching by the Examiner of "some immunologists" is certainly not supported by these cited references which are very clear in their teaching of either triggering immune responses or suppressing immune response.

The combination of the cited references does not teach each and every element of the claimed invention and thus cannot render the claims obvious. In particular, the cited references do not teach or suggest suppressing or reducing an immune response of a mammal to an antigen by the administration of a plant tissue containing the antigen. There is no suggestion provided in the '719 patent to suppress immune response. Similarly, there is no suggestion in the '581 application to provide any plant based antigens for therapy. If there is no suggestion in either cited document then there can be no motivation to combine. As such, the claimed invention cannot be considered, and indeed is not, obvious over the references cited by the Examiner.

In light of the above, the Examiner is respectfully requested to withdraw the rejection under 35 U.S.C. § 103(a).

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this Amendment or Reply, or the application in general, it would be appreciated if the Examiner would

telephone the undersigned attorney concerning such questions so that the prosecution of this application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: July 12, 2004

By: _____
Susan M. Dadio
Registration No. 40,373

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620